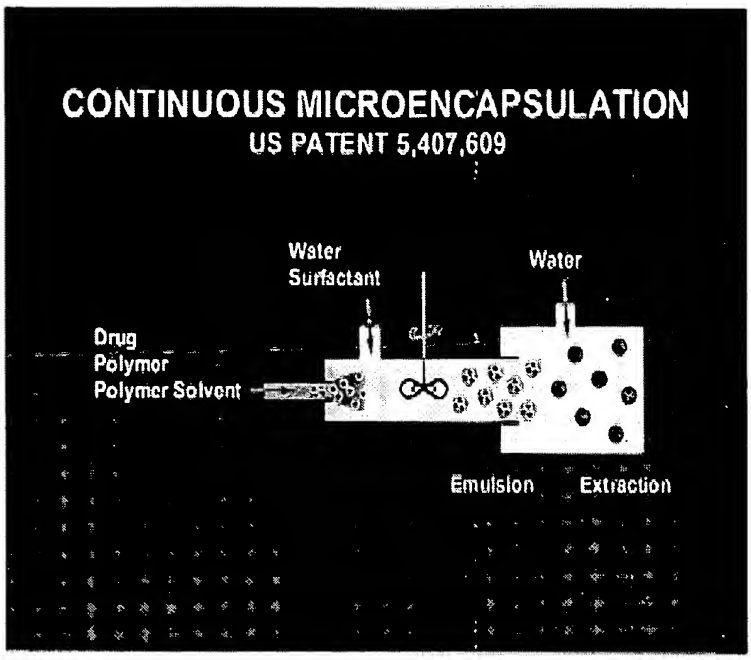


Advantages

- US Patent issued 1995
- Fast encapsulation time -- milliseconds
- Minimal exposure to polymer solvent
- High encapsulation efficiency
- Good Yields
- Makes small microparticles
  <100 micron <10 micron

Drugs Microencapsulated

- Proteins
- Peptides
- Small molecules
- Water-soluble drugs
- Hydrophobic drugs
- Drugs encapsulated in lactide/glycolide polymers

Figure 1

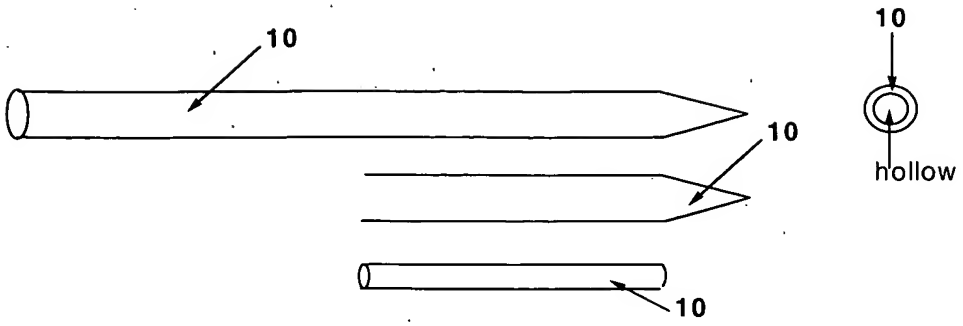


Figure 2

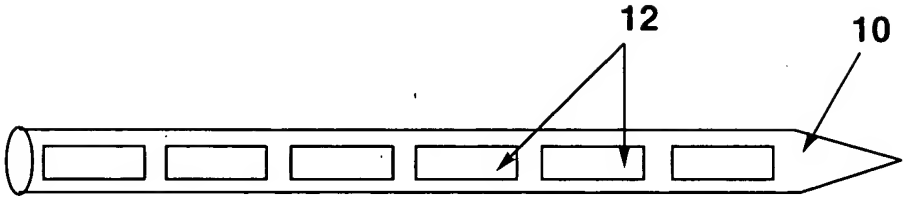


Figure 3

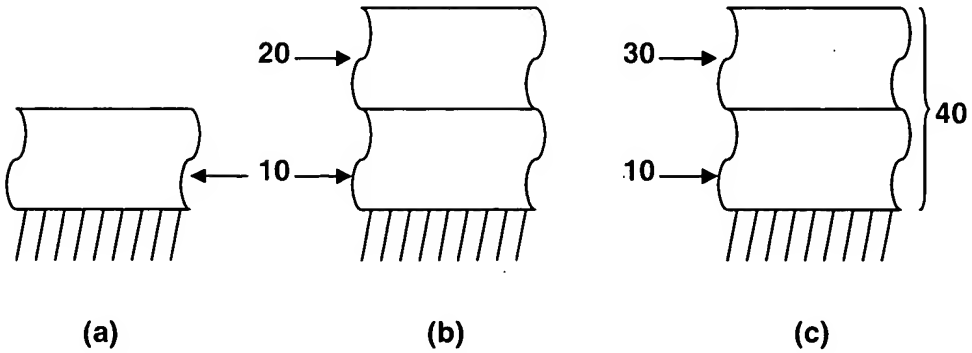


Figure 4

Conditions: Ambient

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Hardness:	F	B	3B	4B	F

Conditions: 5 minutes in 37°C pH 7.4 Saline Buffer

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Hardness:	F	B	9B	<9B	F

Hardness Rating: 2H-H-F-HB-B-2B-3B-4B-5B-6B-7B-8B-9B

Harder ⟷ Softer

Figure 5

Conditions: Ambient

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Resistance To Cracking	< 3 mm	< 3 mm	< 3mm	< 3mm	<3mm

Conditions: 5 minutes in 37°C pH 7.4 Saline Buffer

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Resistance To Cracking	< 3 mm	< 3 mm	< 3mm	< 3mm	< 3mm

Figure 6

Conditions: Ambient

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Class:	5B	5B	5B	4B	5B

Class Rating: 5B = 0% of coating removed from substrate
4B = Less than 5% of coating removed from substrate

Figure 7

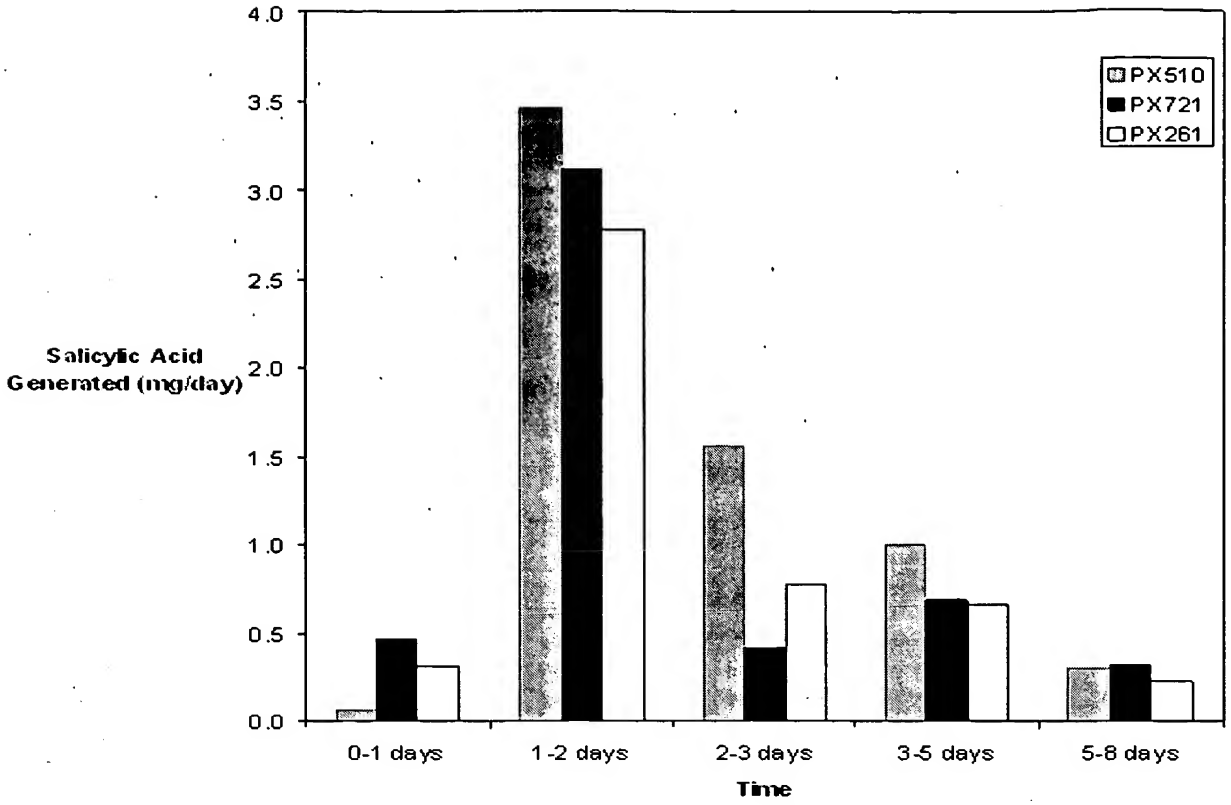


Figure 8A

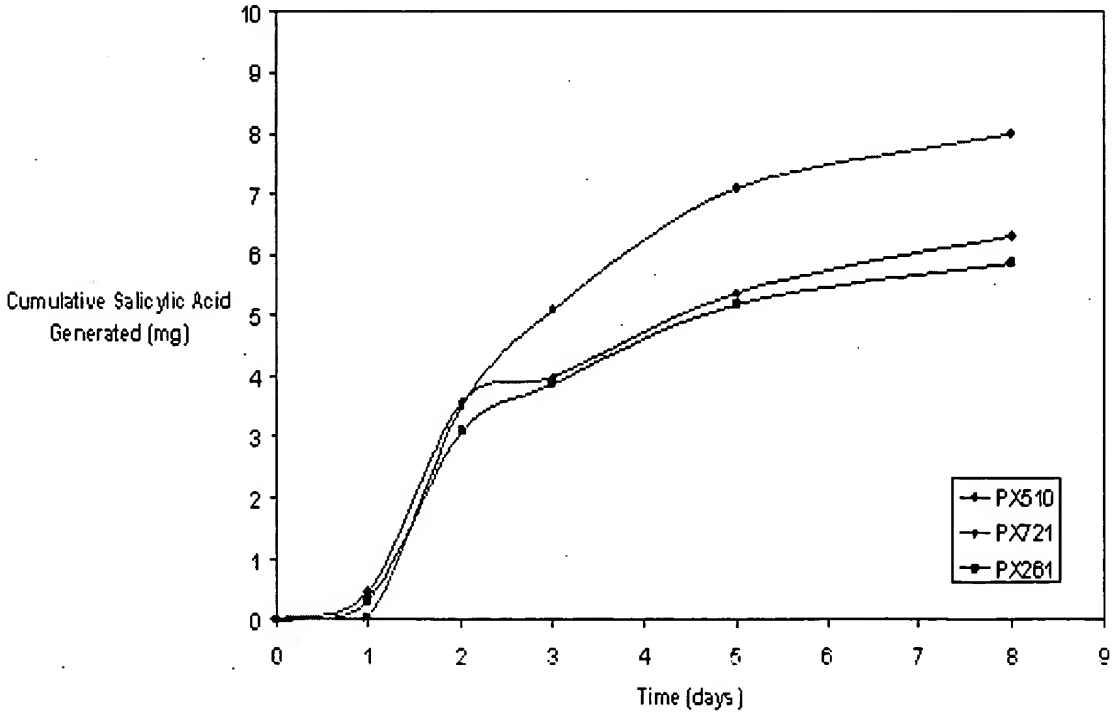


Figure 8B

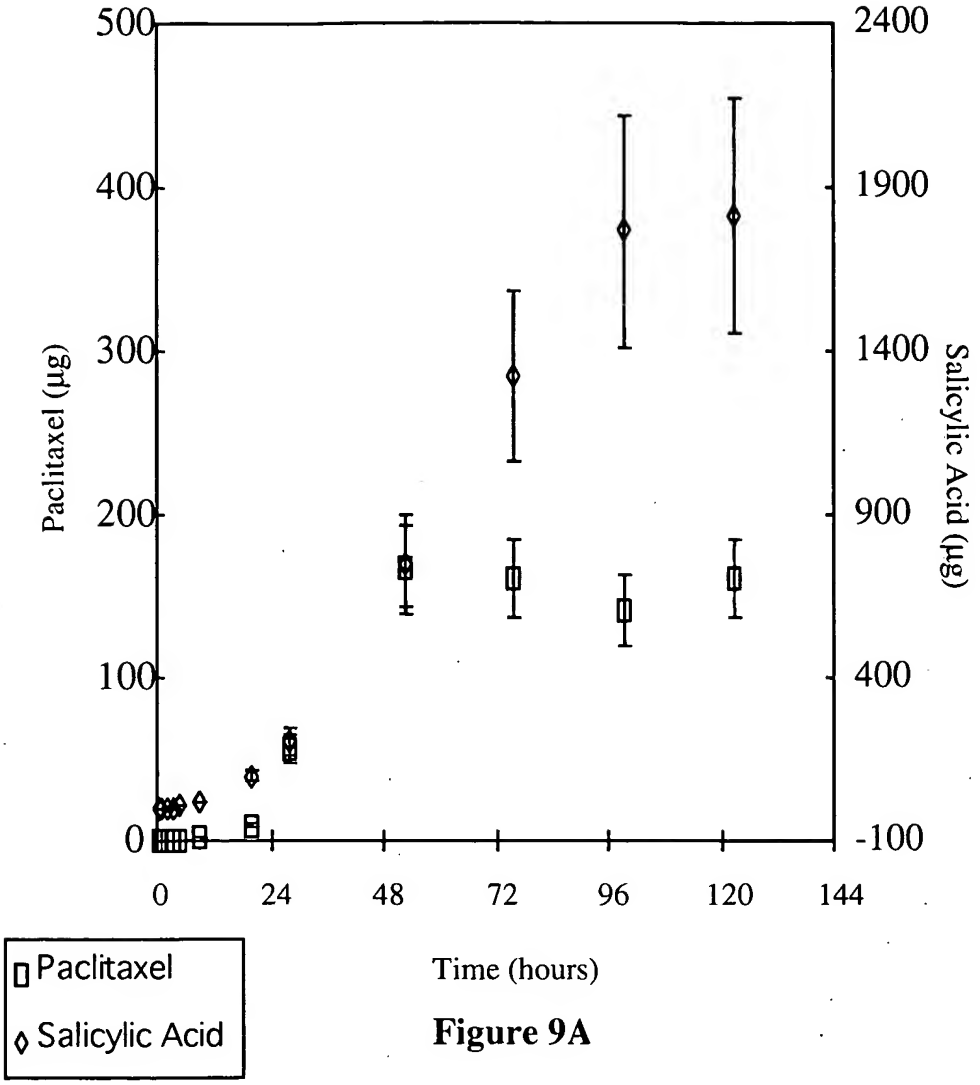

500
400
300
200
100
0
Paclitaxel (µg)
2400
1900
1400
900
400
-100
Salicylic Acid (µg)
0
24
48
72
96
120
144
Time (hours)
Paclitaxel
Salicylic Acid

Figure 9A

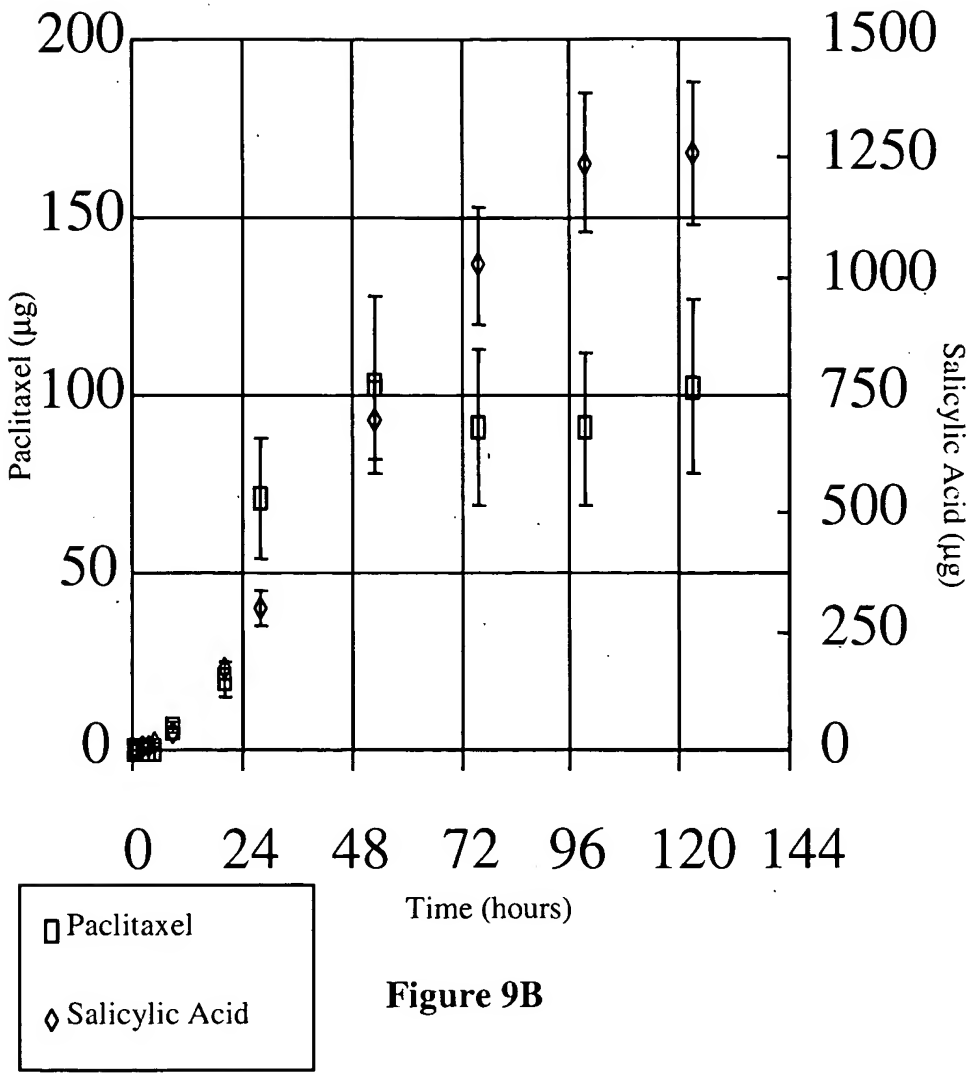

200
150
100
50
0
Paclitaxel (µg)
1500
1250
1000
750
500
250
0
Salicylic Acid (µg)
0
24
48
72
96
120
144
Time (hours)
Paclitaxel
Salicylic Acid

Figure 9B

	Formulation			
Property	PX510	PX721	PX261	PX749
T_g (°C)	44	38	29	16
Tensile modulus (MPa)	2.0 (25 °C) 5.1 (37 °C)			3.0 (25 °C)
Yield Strength (MPa)	Not observed			6.0 (25 °C)
Ultimate Elongation (%)	1.5 (25 °C) 350 (37 °C)			500 (25 °C)

Figure 10

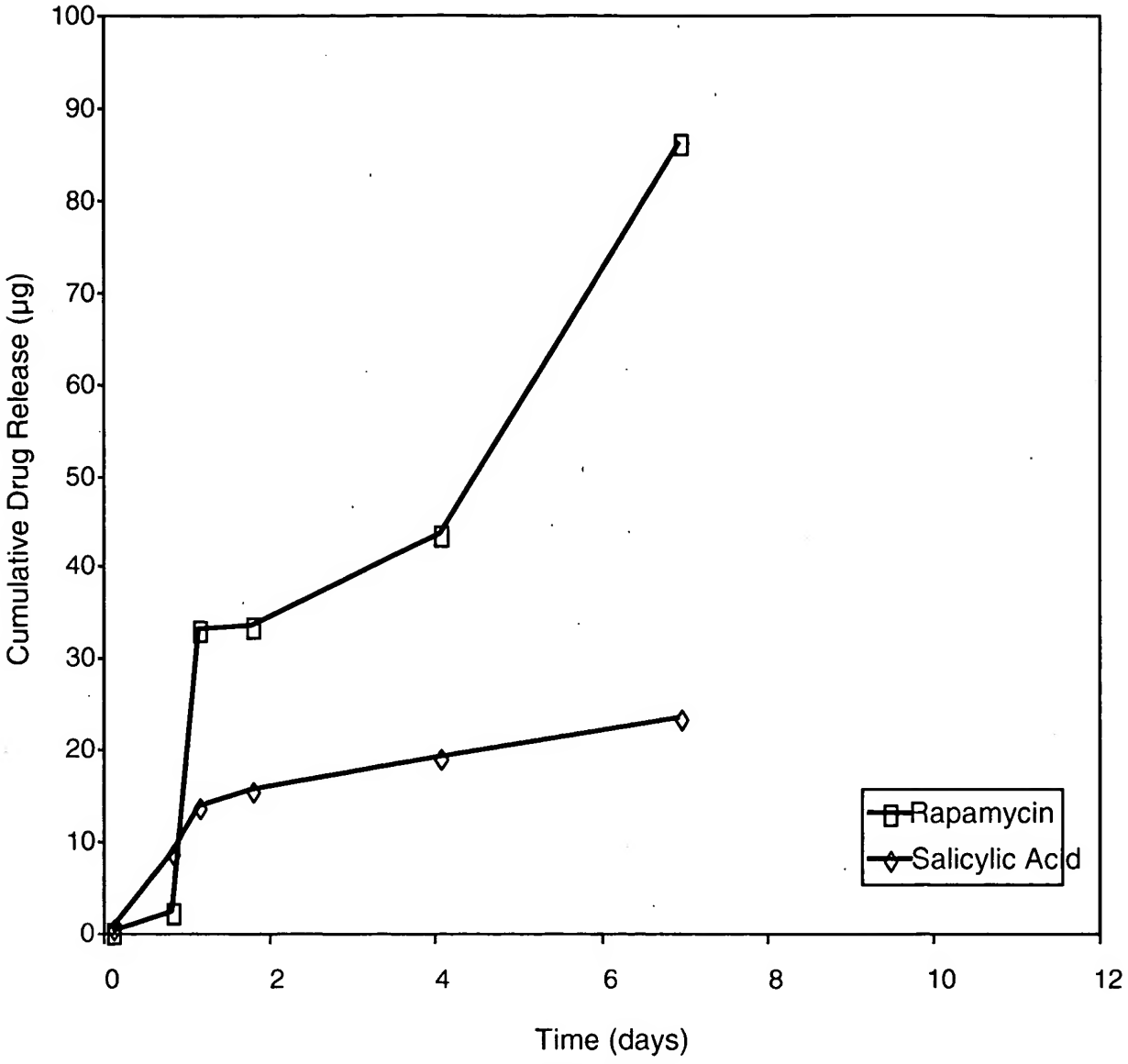

100
90
80
70
60
50
40
30
20
10
0
Cumulative Drug Release (µg)
0
2
4
6
8
10
12
Time (days)
Rapamycin
Salicylic Acid

Figure 11

	E Beam (3 MRad)			γ (25-35 KGys)		
Property	PX510	PX721	PX261	PX510	PX721	PX261
MW	-26%	-39%	-26%	-14%	N/C	N/C
Hardness	-2 units	N/C	-1 unit	N/C	-3 units	-2 units
Flexibility	N/C	N/C	N/C	N/C	N/C	N/C
Adhesion	N/C	N/C	-1 unit	N/C	N/C	N/C

N/C: no change

Figure 12

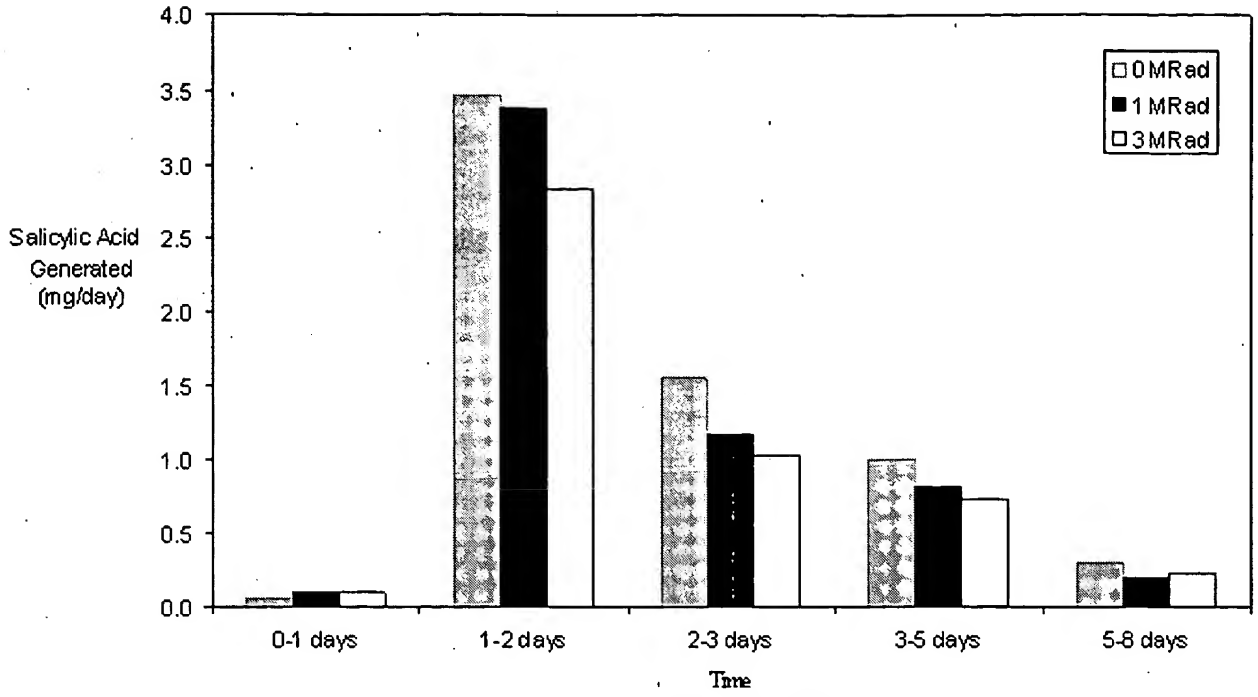


Figure 13A

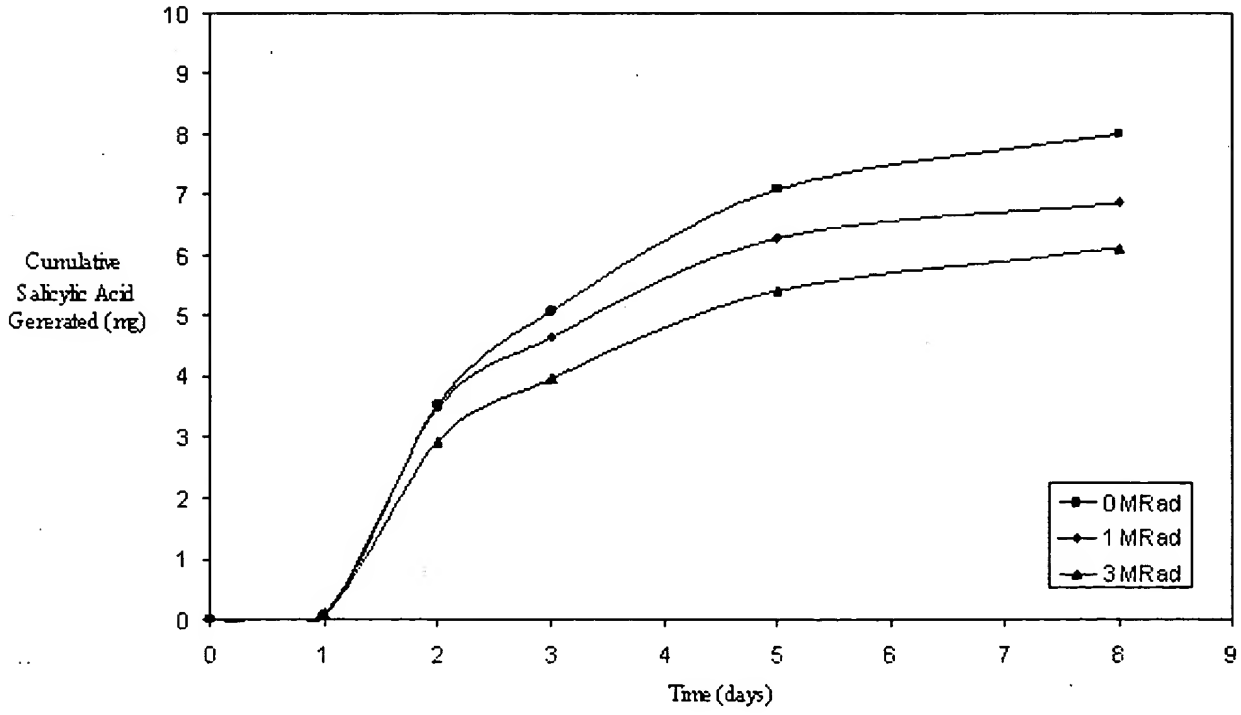


Figure 13B

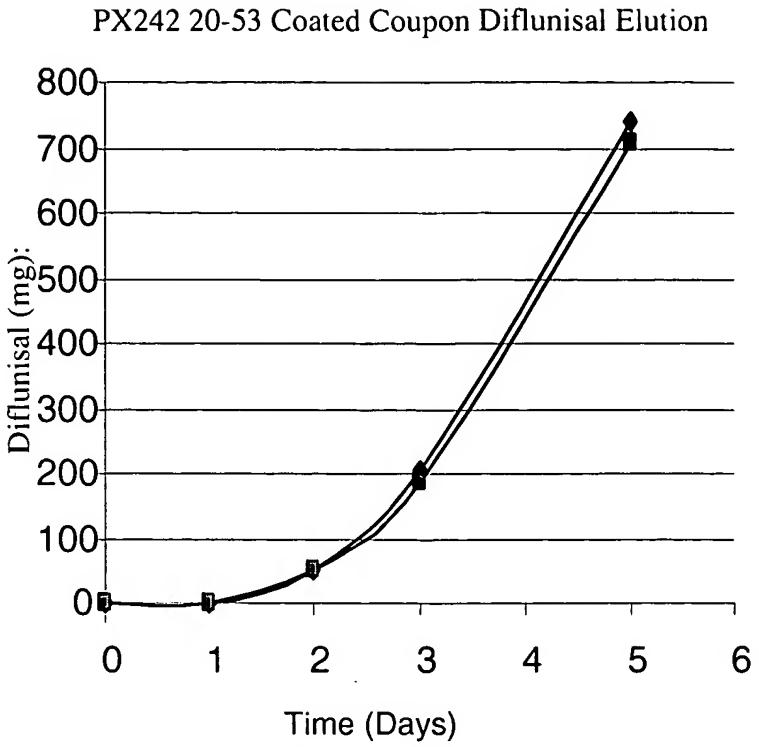


Figure 14

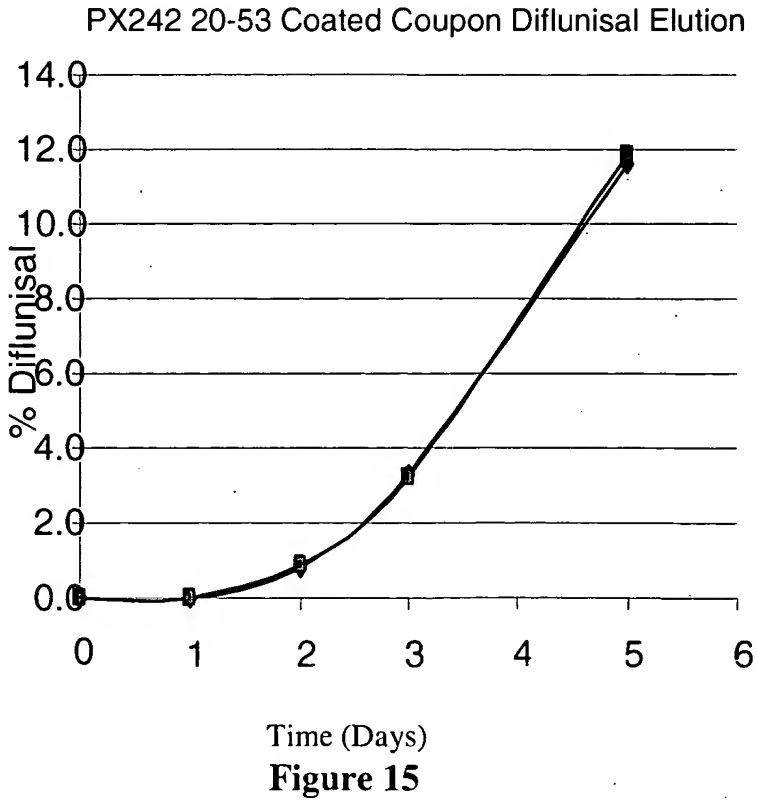


Figure 15

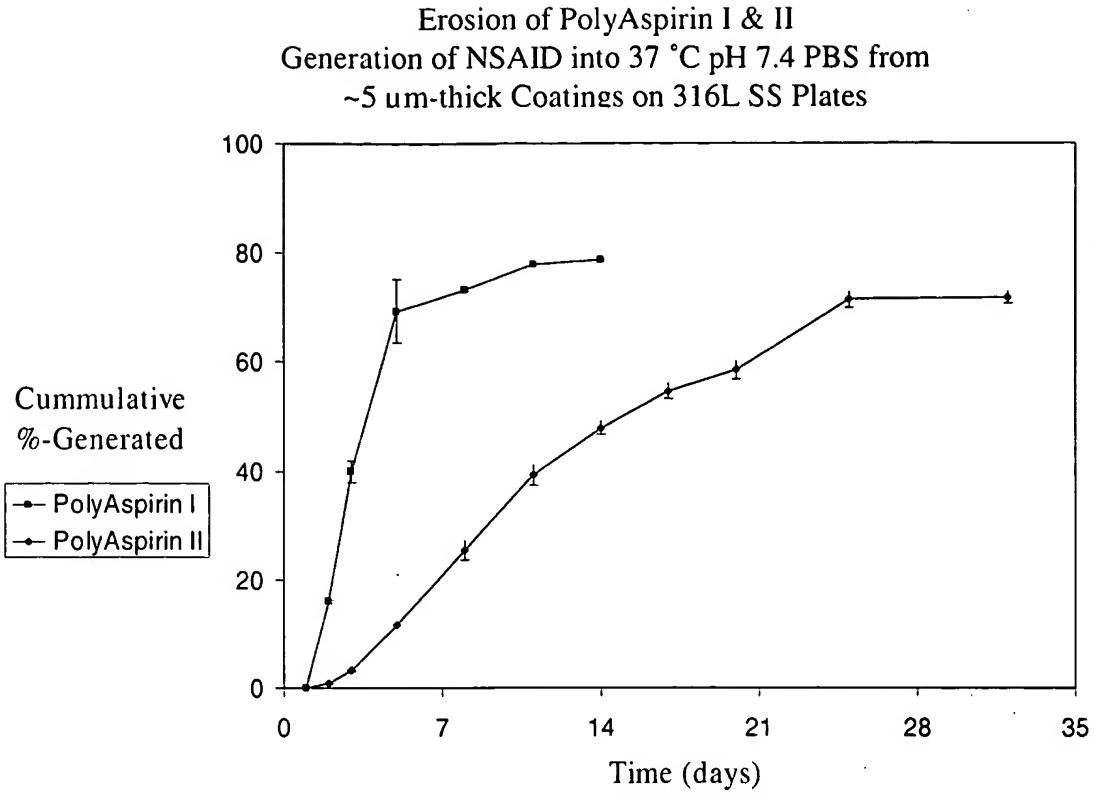


Figure 16

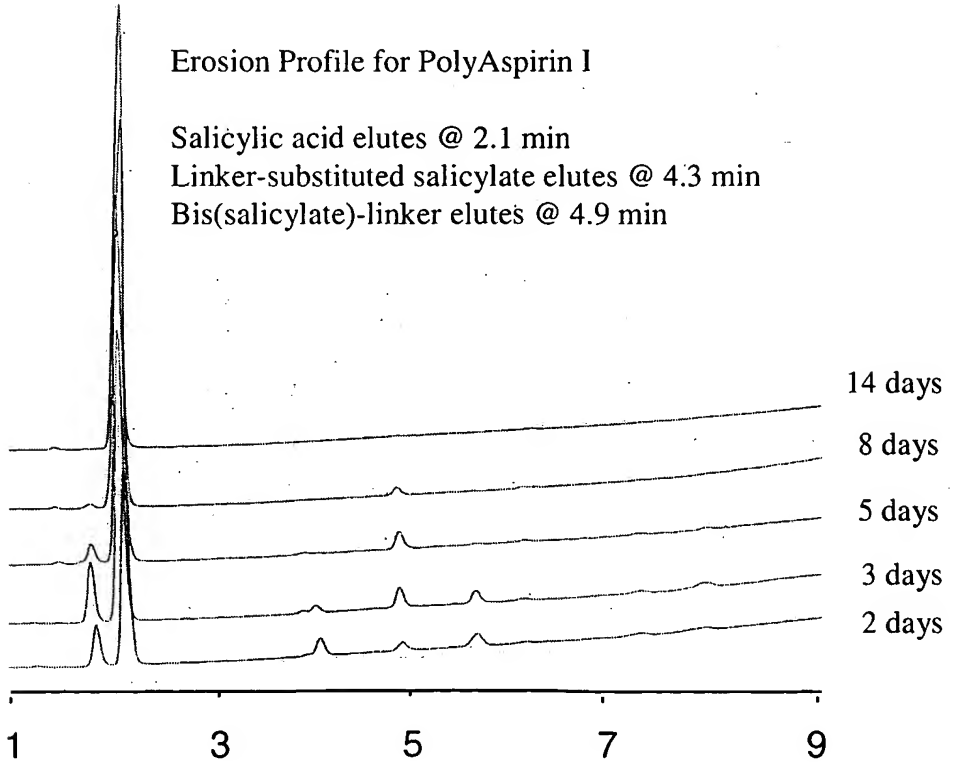


Figure 17

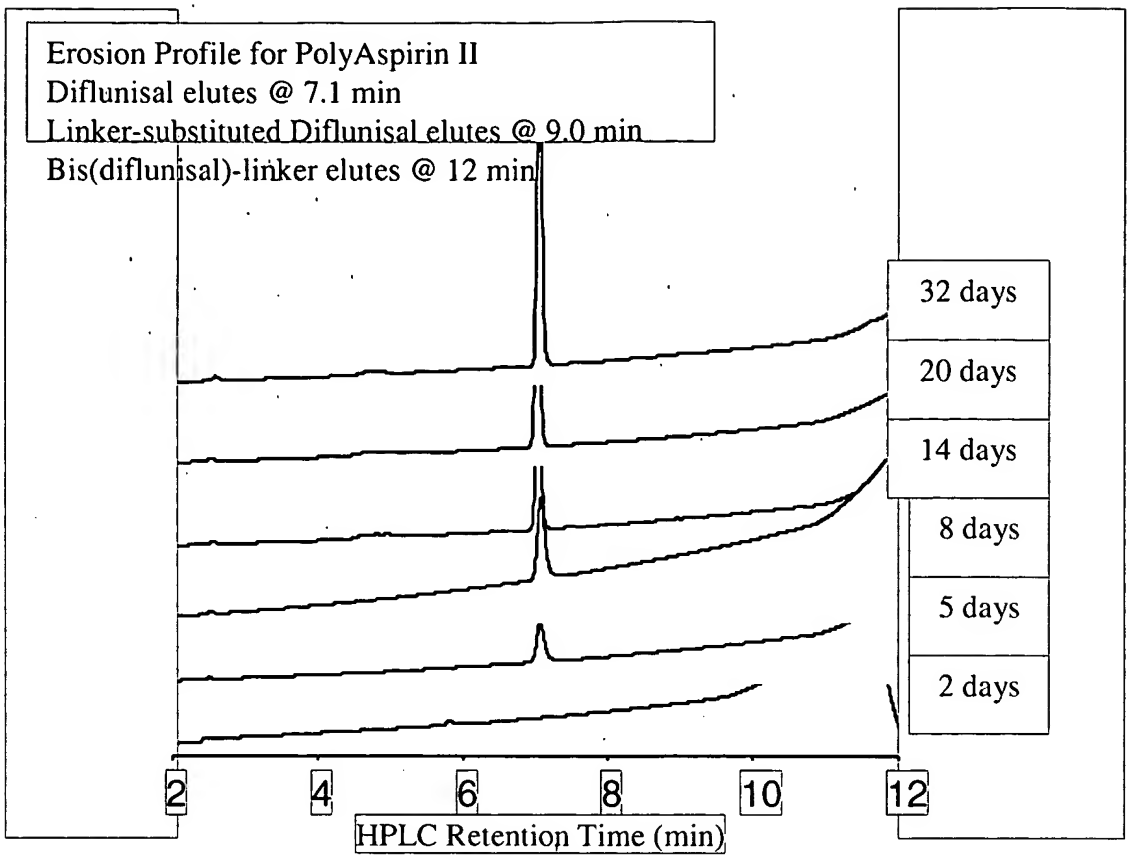


Figure 18

Effect of MW on Erosion
Generation of Diflunisal from PolyAspirin II into 37 °C Serum from Coatings on 316L SS Plates

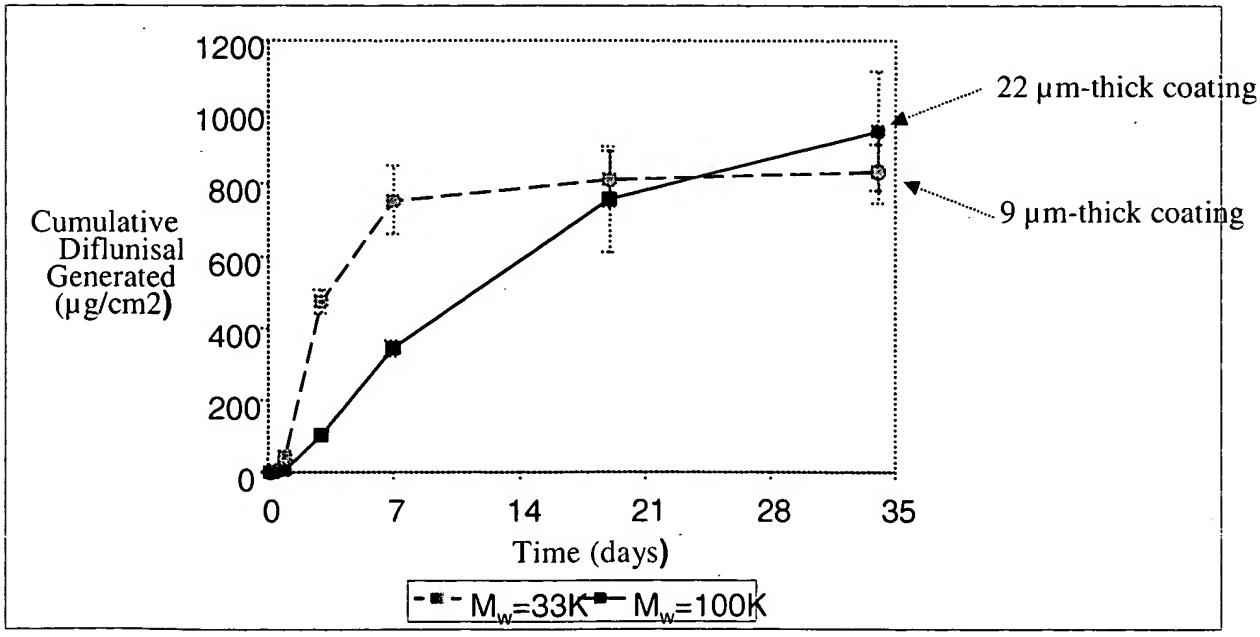


Figure 19

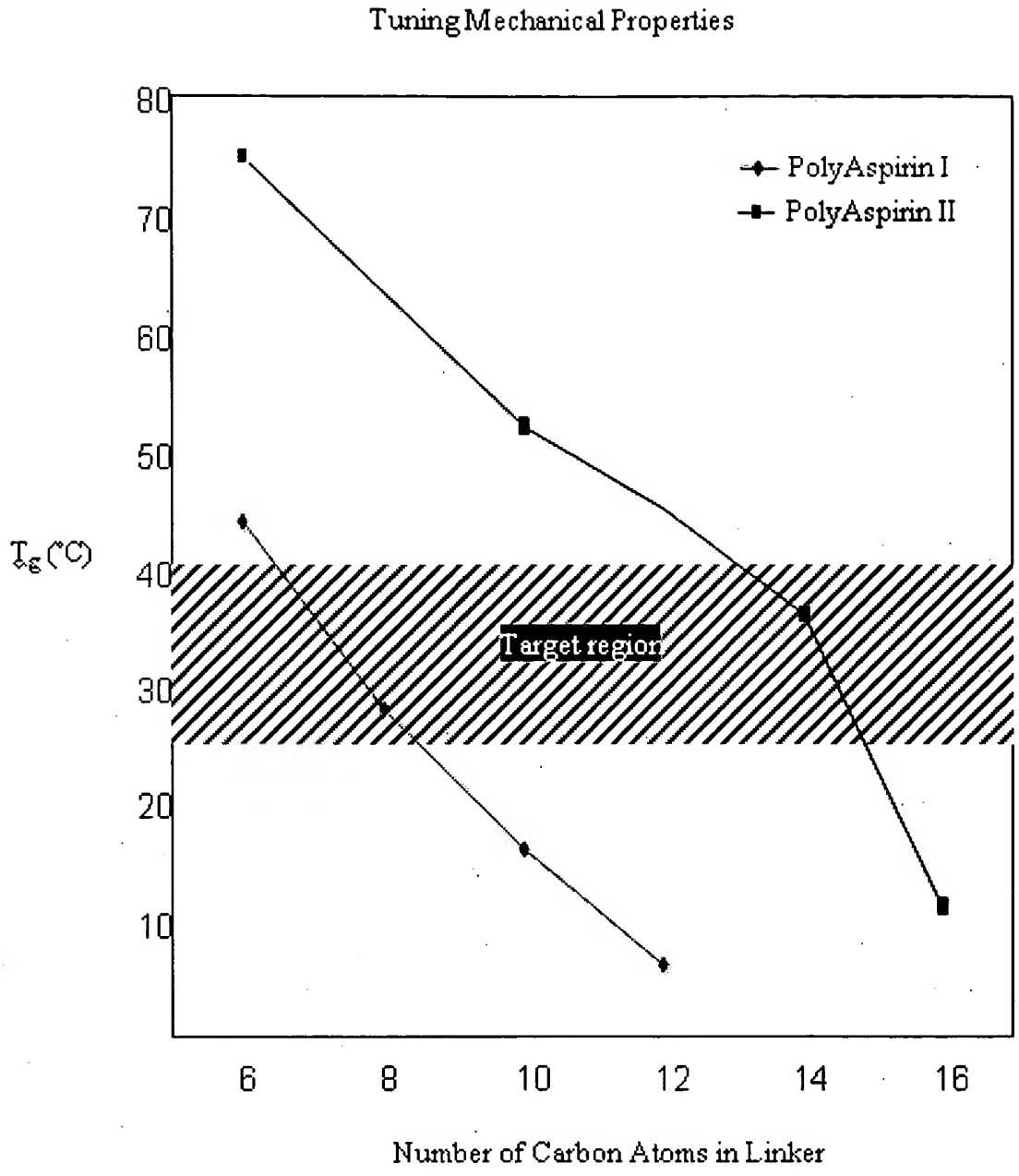

Tuning Mechanical Properties
80
70
60
50
40
30
20
10
T_g (°C)
PolyAspirin I
PolyAspirin II
Target region
6
8
10
12
14
16
Number of Carbon Atoms in Linker

Figure 20

Thermoanalysis of PolyAspirin™

Property	PolyAspirin I	PolyAspirin II	
	PX261	PX657	
	Mw ~ 20K	M_w ~ 33K	M_w ~ 100K
T_g (°C)	29	36	44
Ultimate Stress (kPa)	1700 (25°C) >2000 (37°C)	>2800 (25°C)	>2600 (25°C)
Ultimate Elongation (%)	>500 (25°C) >500 (37°C)	>4 (25°C)	>500 (25°C)
Toughness (kPa)	>3900 (25°C) >4400 (37°C)	>560 (25°C)	>4000 (25°C)

Figure 21

Properties of PolyAspirin™ Coatings

Test	PolyAspirin I	PolyAspirin II	
	PX261	PX657	
	Mw ~ 20K	Mw ~ 33K	Mw ~ 100K
<u>Hardness</u>			
Ambient	B	F	3H
5 min in PBS, 37 °C	B	2B	B
1 hr in PBS, 37 °C	-	8B	4B
<u>Flexibility</u>			
Ambient	<3 mm	<3 mm	<3 mm
5 min in PBS, 37 °C	<3 mm	<3 mm	<3 mm
1 hr in PBS, 37 °C	-	<3 mm	<3 mm
<u>Adhesion</u>			
Ambient	5B	5B	5B

Figure 22

PolyAspirin Coatings with Admixtures

Test	PolyAspirin II (PX657)	
	No Admixture	20% Paclitaxel Admixed
<u>Hardness</u>		
Ambient	F	F
5 min in PBS, 37 °C	2B	F
1 hr in PBS, 37 °C	8B	6B
<u>Flexibility</u>		
Ambient	<3 mm	<3 mm
5 min in PBS, 37 °C	<3 mm	<3 mm
1 hr in PBS, 37 °C	<3 mm	<3 mm
<u>Adhesion</u>		
Ambient	5B	5B

Figure 23

Erosion of PolyAspirin I & II

Diflunisal Generation & Paclitaxel Release into 37 °C Serum from ~5 µm-thick Coatings on 316L SS Plates

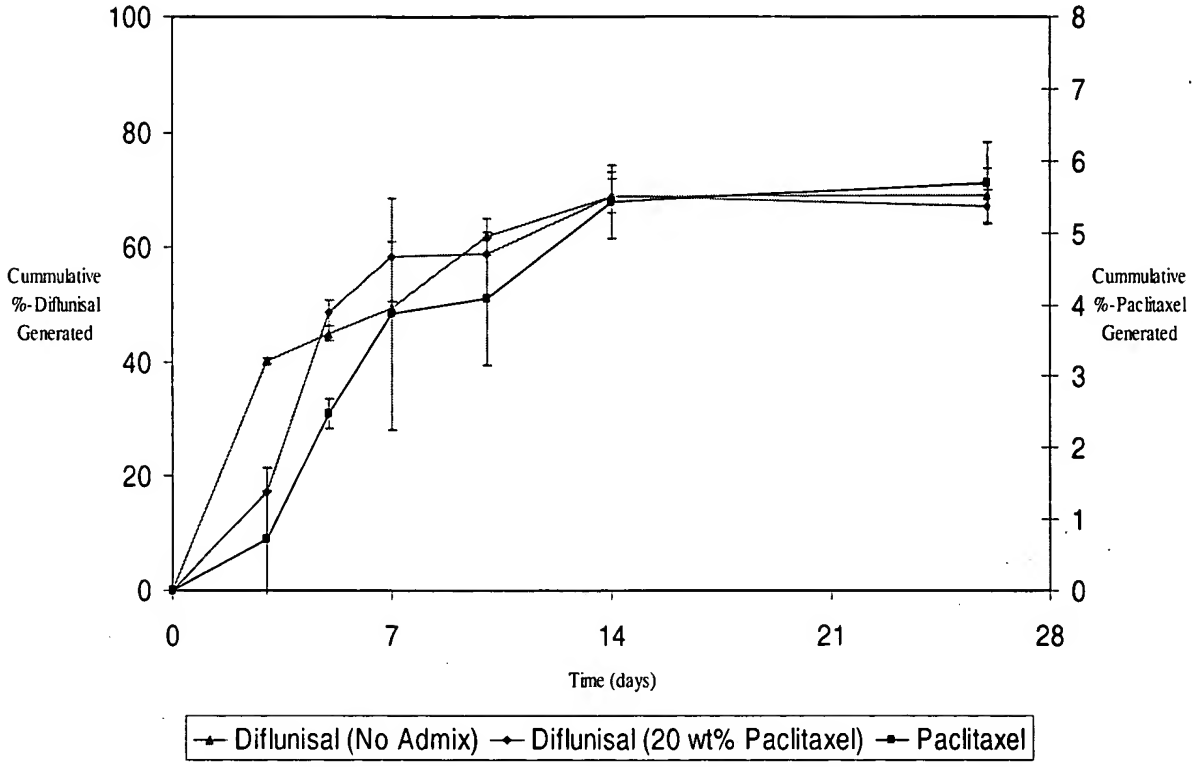


Figure 24

Erosion of Sterilized PolyAspirin II

Generation of Diflunisal into 37 °C Serum from ~5 μm-thick Coatings on 316L SS Plates

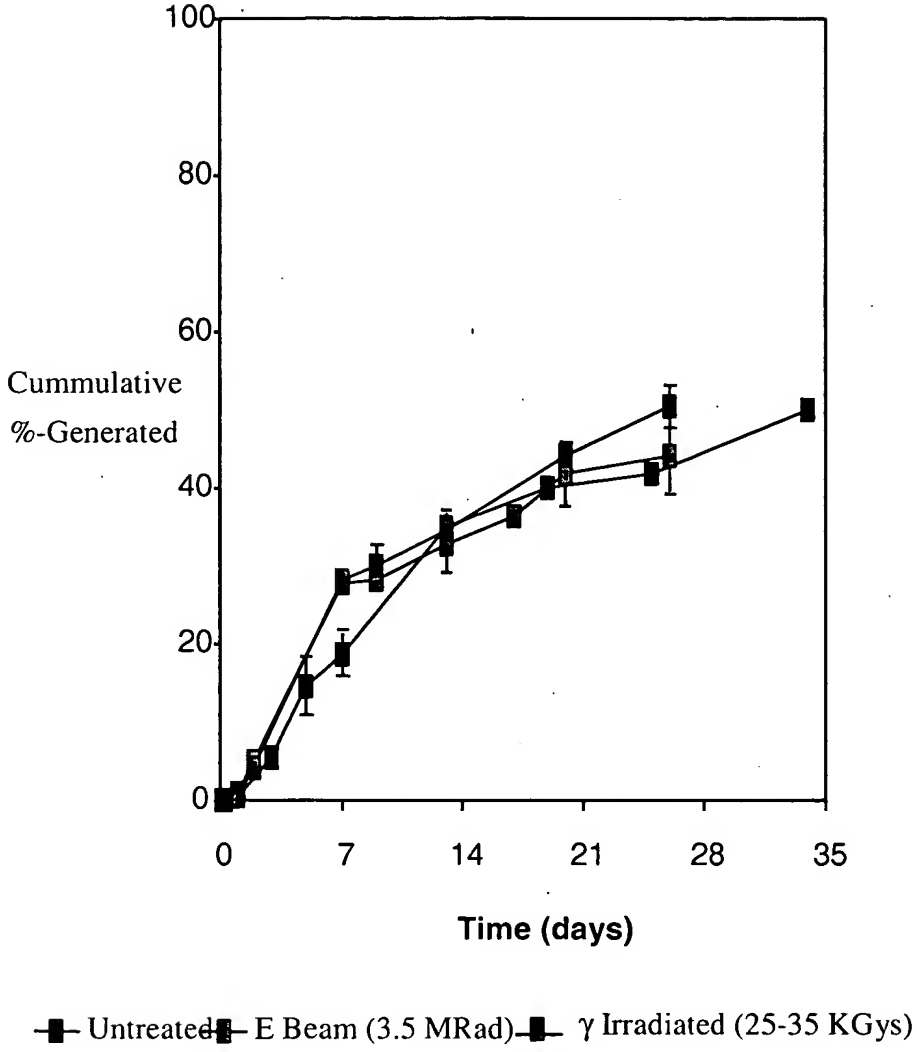


Figure 25

γ Irradiation (25-35 Kgys)

N/C: no change	PolyAspirin I	PolyAspirin II
Property	PX261 M_w ~ 20K	PX657 M_w ~ 100K
MW	N/C	-50%
Hardness	-2 units	-3 units
Flexibility	N/C	-
Adhesion	N/C	-

Figure 26

E Beam (3-4.5 MRad)

	PolyAspirin I	PolyAspirin II	
Property	PX261 M_w ~ 20 K	PX657 M_w ~ 33K	M_w ~ 80K
MW	-26%	+5%	-30%
Hardness	-1 unit	+2 units	N/C
Flexibility	N/C	-	N/C
Adhesion	-1 unit	-	-

Figure 27

Kinetics of NSAID Generation

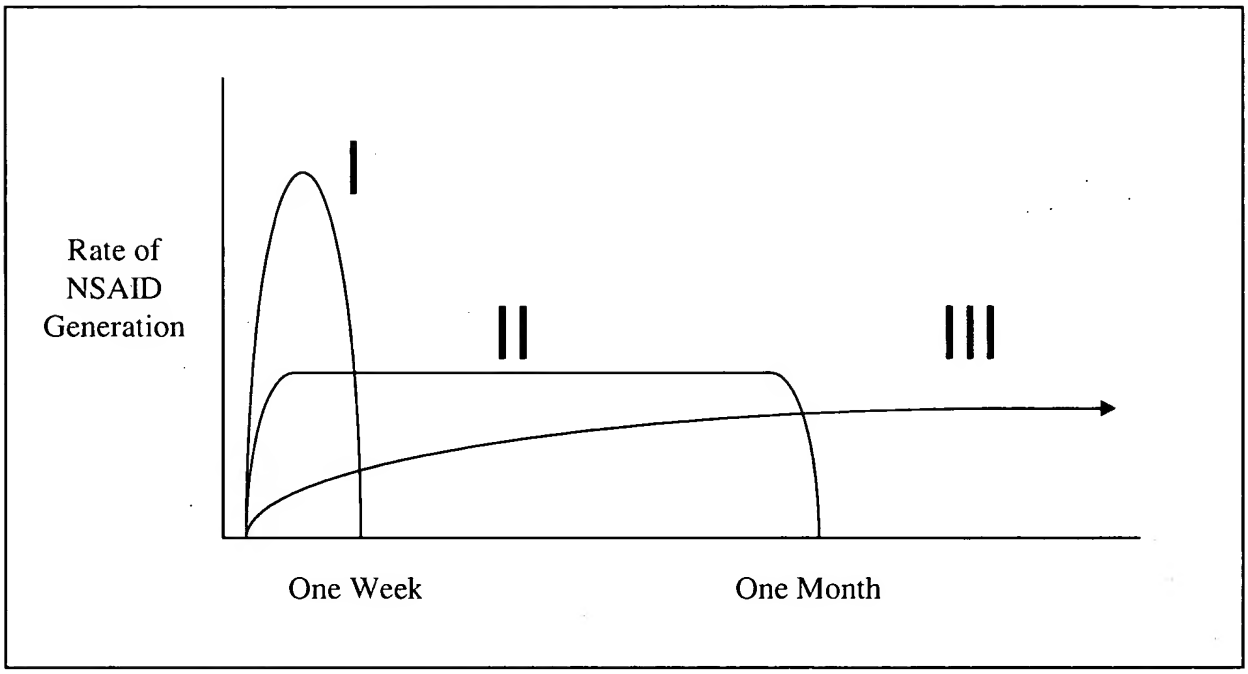


Figure 28

Figure 29

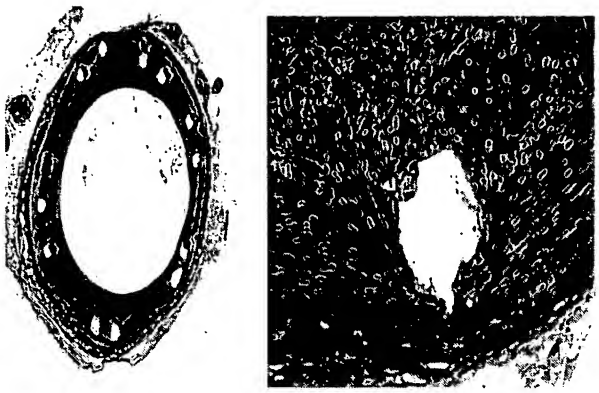


Figure 30

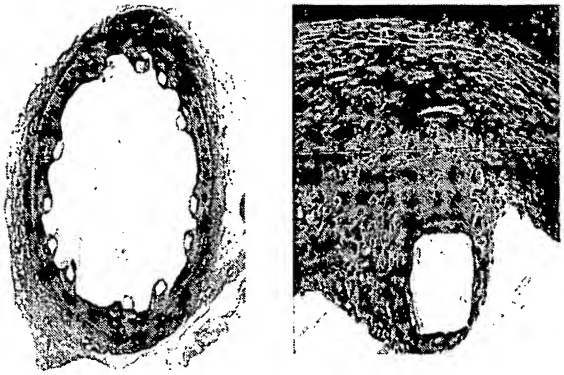


Figure 31

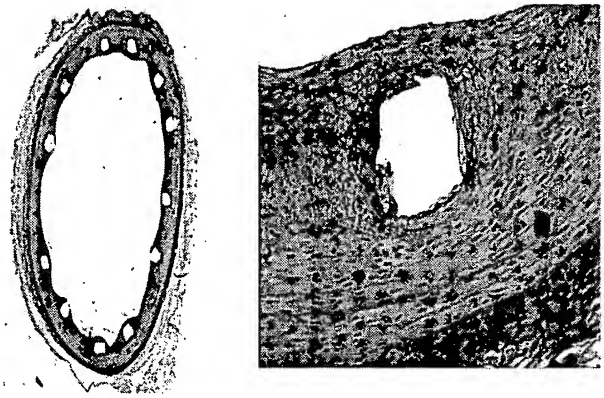


Figure 32

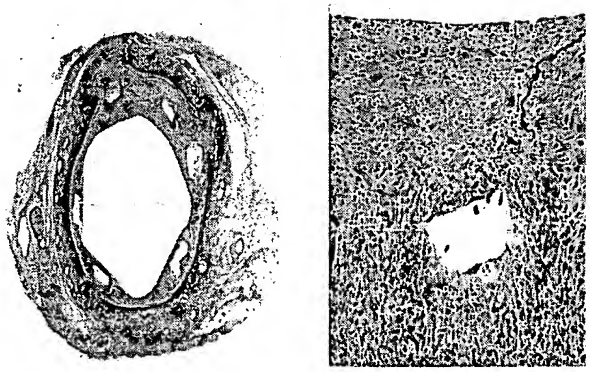


Figure 33

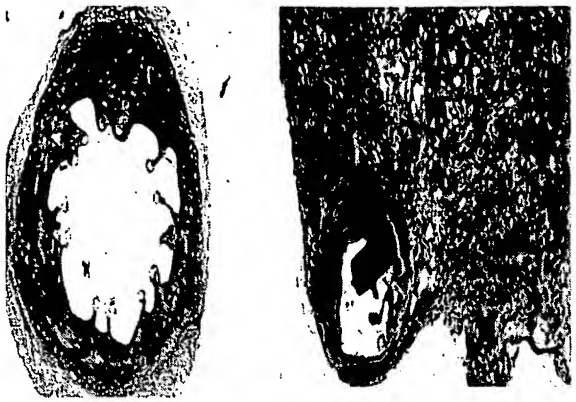


Figure 34

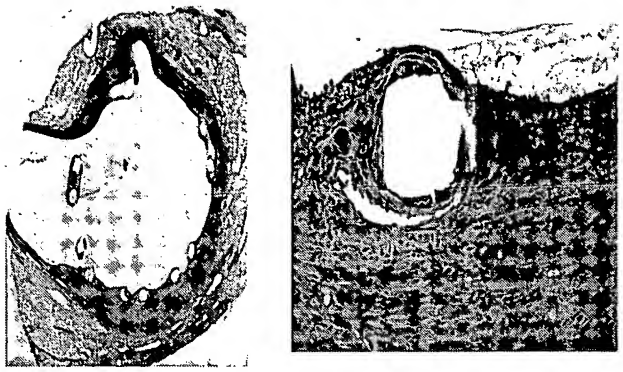
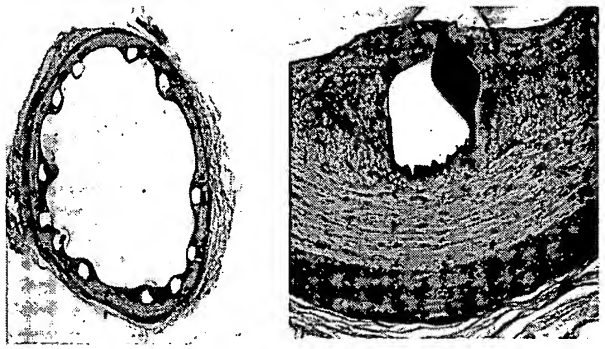


Figure 35



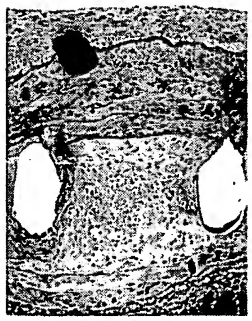


Figure 36

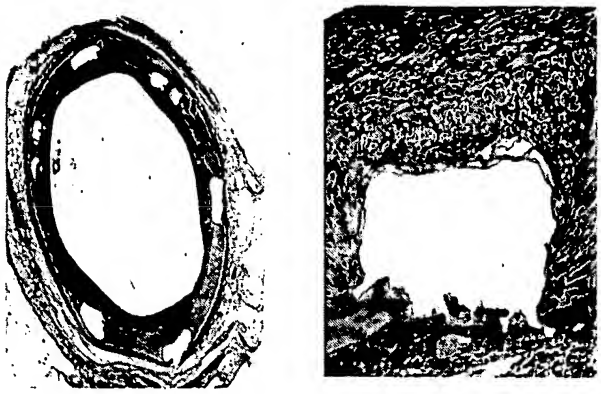


Figure 37

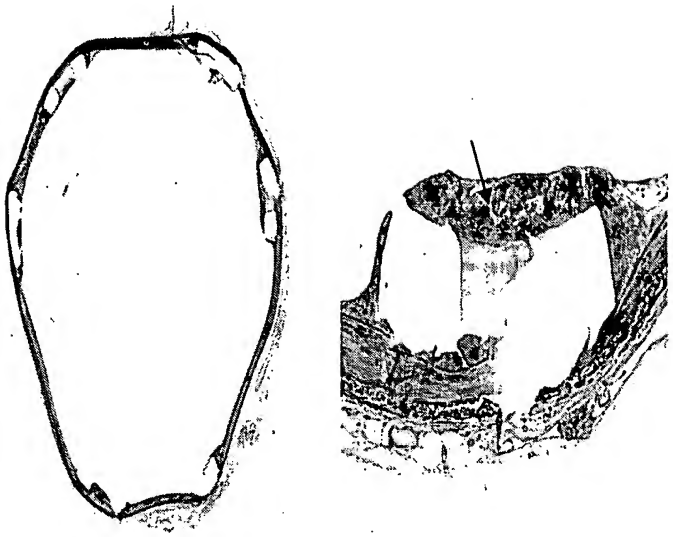


Figure 38

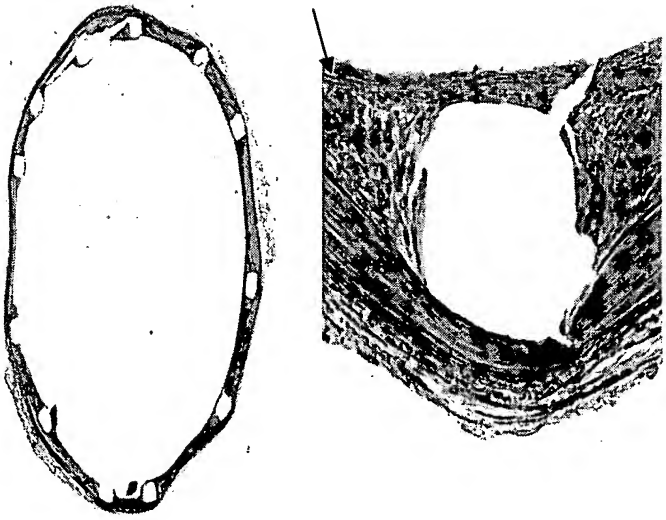


Figure 39

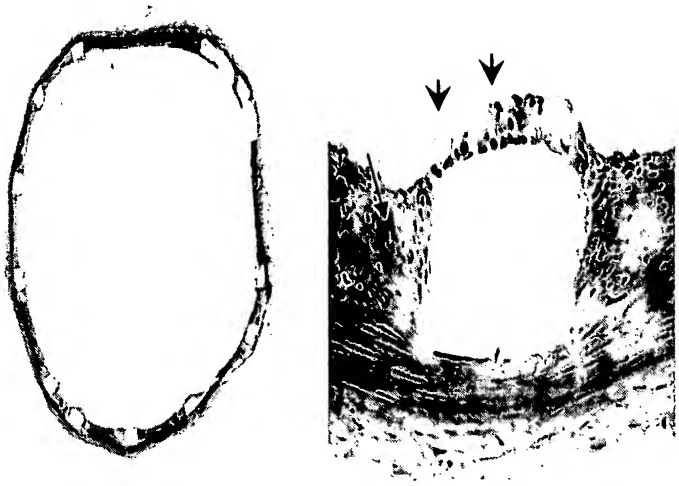


Figure 40

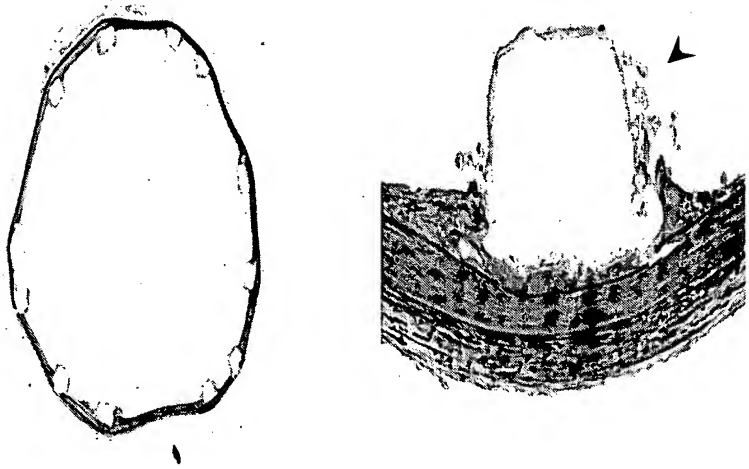


Figure 41

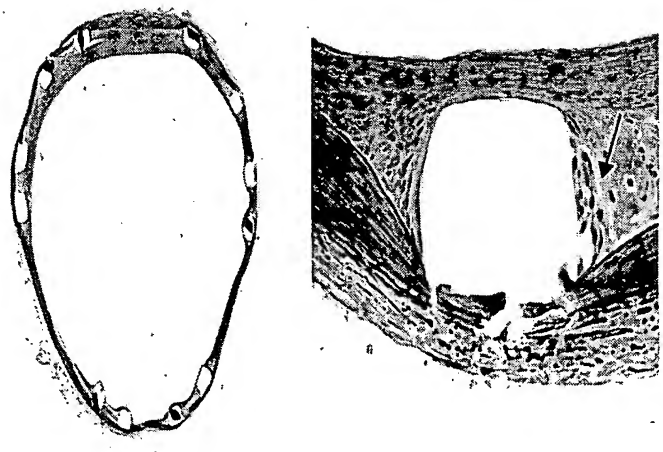


Figure 42

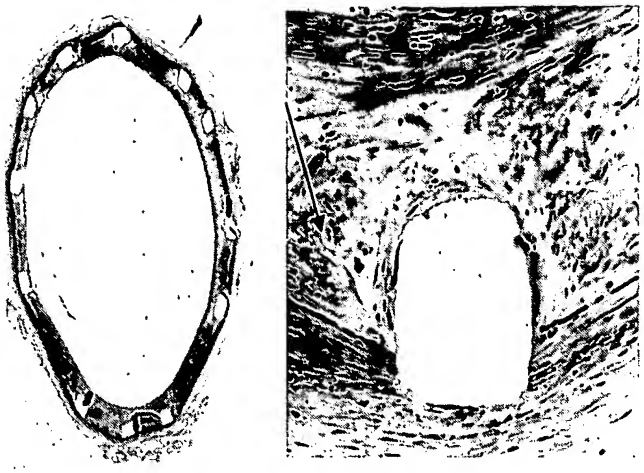
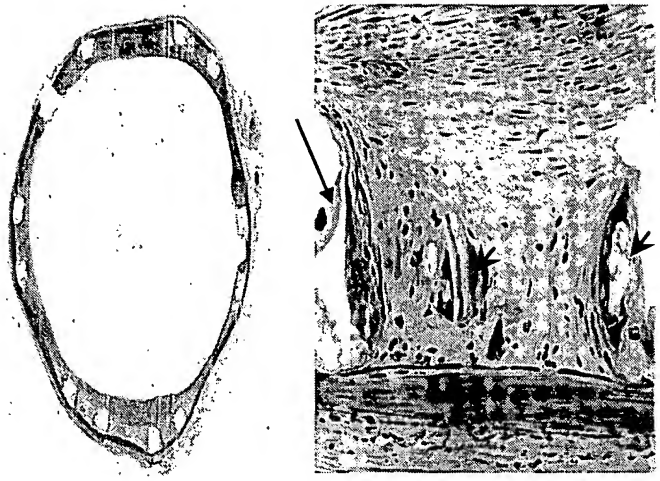


Figure 43



uncrimped/unexpanded

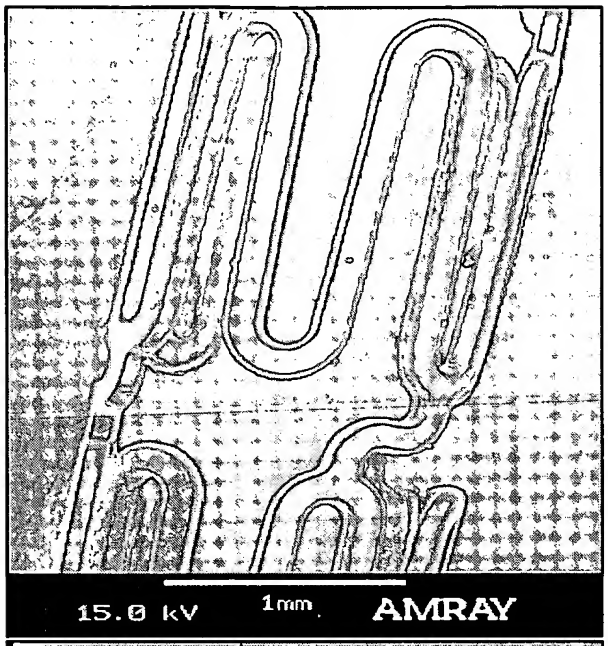


Fig. 44a

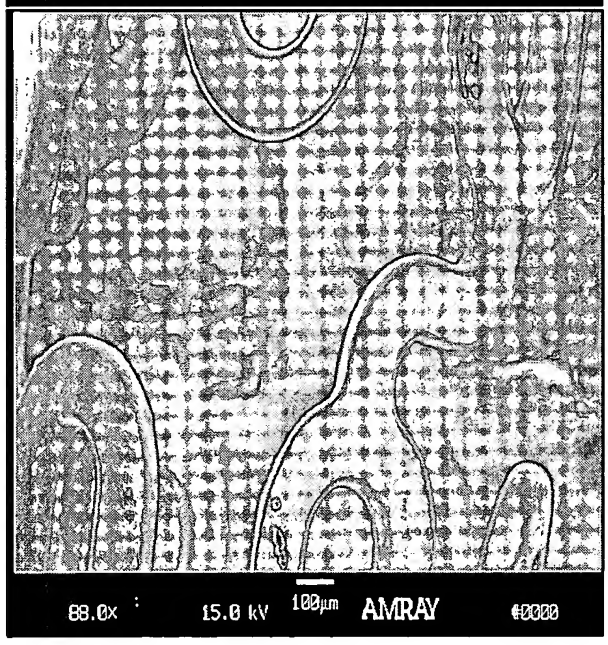


Fig. 44b

Figure 44

uncrimped/unexpanded

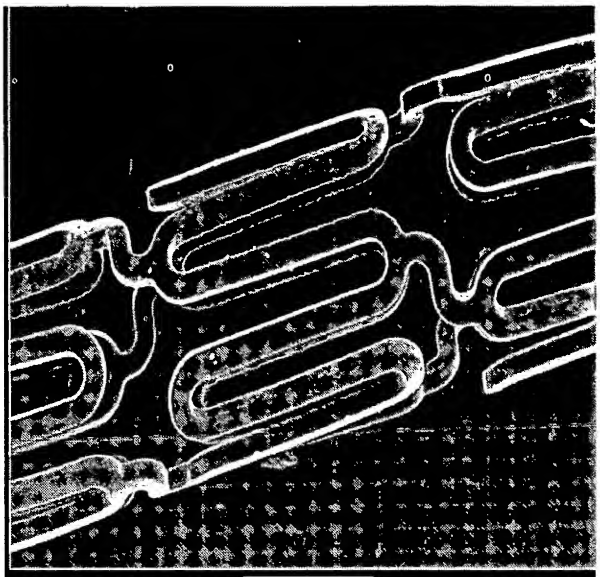


Fig. 45a

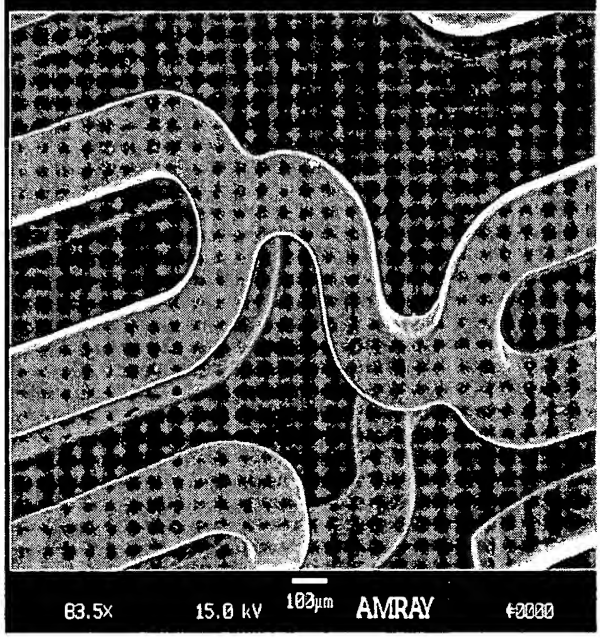


Fig. 45b

Figure 45

Uncrimped/unexpanded

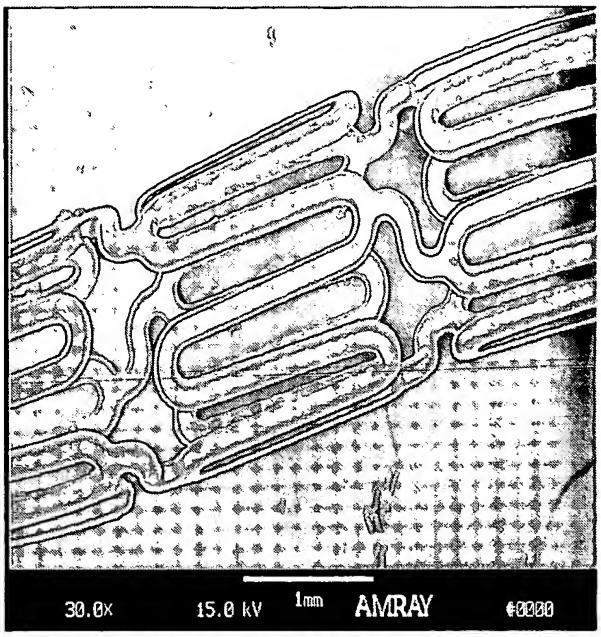


Fig. 46a

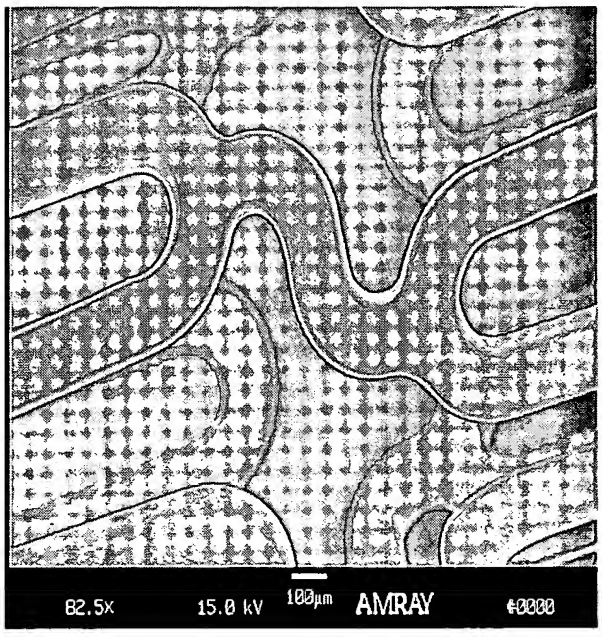


Fig. 46b

Figure 46